PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	Prior Group Art Unit: 1655
Hajime Matsuzaki, *et al.*	)	Prior Examiner F. Lu:
Continuation of Application Serial No.: 09/099,301	)	Atty. Dkt. No. 003848.00099
Filed: November 21, 2001	)	

For: METHODS AND COMPOSITIONS FOR MULTIPLEX AMPLIFICATION OF NUCLEIC ACIDS

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents
Washington, D. C. 20231

Sir:

Preliminarily to the examination of the above-identified application, kindly amend the application as follows. Appendix I is a marked up version of the specification and claims to show changes made.

IN THE SPECIFICATION:

Please amend the paragraph beginning page 1, line 4 to read as follows:

This application is a continuation of U.S. Serial Number 09/099,301, filed June 18, 1998, which claims priority to U.S. Provisional Application, Serial No. 60/050,405, filed on June 20, 1997, the text of which is expressly incorporated herein.

Please amend the specification at page 6, lines 4-23 to read as follows:

Exon 2: 5'-TCATGCTGGATCCCCACTTTTCCTCTTG-3' (SEQ ID NO: 1)

5'TGGCCTGCCCTTCCAATGGATCCACTCA-3' (SEQ ID NO: 2)

Exon 3: 5'-AATTCATGGGACTGACTTTCTGCTCTTGTC-3' (SEQ ID NO: 3)
5'-TCCAGGTCCCAGCCCAACCCTTGTCC-3' (SEQ ID NO: 4)

Exon 4: 5'-GTCCTCTGACTGCTCTTTTCACCCATCTAC-3' (SEQ ID NO: 5)
5'-GGGATACGGCCAGGCATTGAAGTCTC-3' (SEQ ID NO: 6)

Exon 5: 5'-CTTGTGCCCTGACTTTCAACTCTGTCTC-3' (SEQ ID NO: 7)
5'-TGGGCAACCAGCCCTGTCGTCTCTCCA-3' (SEQ ID NO: 8)

Exon 6: 5'-CCAGGCCTCTGATTCCTCACTGATTGCTC-3' (SEQ ID NO: 9)
5'-GCCACTGACAACCACCCTTAACCCCTC-3' (SEQ ID NO: 10)

Exon 7: 5'-GCCTCATCTTGGGCCTGTGTTATCTCC-3' (SEQ ID NO: 11)
5'-GGCCAGTGTGCAGGGTGGCAAGTGGCTC-3' (SEQ ID NO: 12)

Exon 8: 5'-GTAGGACCTGATTTCCTTACTGCCTCTTGC-3' (SEQ ID NO: 13)
5'-ATAACTGCACCCTTGGTCTCCTCCACCGC-3' (SEQ ID NO: 14)

Exon 9: 5'-CACTTTTATCACCTTTCCTTGCCTCTTTCC-3' (SEQ ID NO: 15)
5'-AACTTTCCACTTGATAAGAGGTCCCAAGAC-3' (SEQ ID NO: 16)

Exon 10: 5'-ACTTACTTCTCCCCCTCCTCTGTTGCTGC-3' (SEQ ID NO: 17)
5'-ATGGAATCCTATGGCTTTCCAACCTAGGAAG-3' (SEQ ID NO: 18)

Exon 11: 5'-CATCTCTCCTCCCTGCTTCTGTCTCCTAC-3' (SEQ ID NO: 19)
5'-CTGACGCACACCTATTGCAAGCAAGGGTTC-3' (SEQ ID NO: 20)

IN THE CLAIMS:

Please cancel claims 12-14. Please amend claims 1, 10, 11, 13, and 15.

1. (Amended) A method of performing multiple polymerase chain reactions in a single vessel, comprising:

priming DNA synthesis of at least two amplicons on a template in a vessel with at least two sets of primers, wherein the primers are present in the vessel at a predetermined molar ratio, wherein the molar ratio is described by:

$$C_A = C_L (L_A \div L_L)^2$$

wherein C_A is the concentration of primers for an amplicon A; wherein C_L is the concentration of primer for the longest amplicon; wherein L_A is the length of the amplicon A; and wherein L_L is the length of the longest amplicon, and wherein the amplicons are distinct.

10. (Amended) The method of claim 9 wherein the primers are present in the following molar ratios: exon 2 (89.4): exon 3 (26.9): exon 4 (450): exon 5 (245.8): exon 6 (138.3): exon 7 (101.8): exon 8 (193.0): exon 9 (70.8): exon 10 (146.5): exon 11 (177.3).

11. (Amended) A method of performing multiple polymerase chain reactions in a single vessel, comprising:

priming DNA synthesis on a genomic p53 template in a vessel with ten sets of primers which amplify exons 2-11 of p53, wherein the primers are shown in SEQ ID NOS: 1-20, wherein the primers are present in the vessel at the following molar ratios: exon 2 (89.4), exon 3 (26.9), exon 4 (450), exon 5 (245.8), exon 6 (138.3), exon 7 (101.8), exon 8 (193.0), exon 9 (70.8), exon 10 (146.5), exon 11 (177.3).

13. (Amended) The kit of claim 12 wherein the molar ratio of the concentrations of the primers is described by:

$$C_A = C_L (L_A \div L_L)^2$$

wherein C_A is the concentration of primers for an amplicon A; wherein C_L is the concentration of primer for the longest amplicon; wherein L_A is the length of the amplicon A; and wherein L_L is the length of the longest amplicon.

15. (Amended) A composition of primers for performing multiplex polymerase chain reaction of at least two amplicons, wherein the primers consist of a mixture at a predetermined molar ratio to each other, wherein the molar ratio of the concentrations of the primers is described by:

$$C_A = C_L (L_A \div L_L)^2$$

wherein C_A is the concentration of primers for an amplicon A; wherein C_L is the concentration of primer for the longest amplicon; wherein L_A is the length of the amplicon A; and wherein L_L is the length of the longest amplicon, wherein the amplicons are distinct.

REMARKS

Entry of the amendments is respectfully requested.

It is believed that no fee is required to make this a complete and timely filing. However, if a fee is required, the Commissioner is authorized to charge Deposit Account No. 19-0733.

Respectfully submitted,

Dated: November 21, 2001

By: _____
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APPENDIX I. MARKED UP VERSION OF SPECIFICATION AND CLAIMS TO SHOW CHANGES MADE

The specification at the paragraph beginning page 1, line 4.

This application is a continuation of U.S. Serial Number 09/099,301, filed June 18, 1998, which claims priority to U.S. Provisional Application, Serial No. 60/050,405, filed on June 20, 1997, the text of which is expressly incorporated herein.

The specification at page 6, lines 4-23.

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Exon 8: 5'-GTAGGACCTGATTTCCTTACTGCCTCTTGC-3' (SEQ ID NO: 13)

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Exon 11: 5'-CATCTCTCCTCCCTGCTTCTGTCTCCTAC-3' (SEQ ID NO: 19)
5'-CTGACGCACACCTATTGCAAGCAAGGGTTC-3' (SEQ ID NO: 20)

The claims

1. (Amended) A method of performing multiple polymerase chain reactions in a single vessel, comprising:

priming DNA synthesis of at least two amplicons on a template in a vessel with at least two sets of primers, wherein the primers are present in the vessel at a predetermined molar ratio, wherein the molar ratio is described by:

$$C_A = C_L (L_A \div L_L)^2$$

wherein C_A is the concentration of primers for an amplicon A; wherein C_L is the concentration of primer for the longest amplicon; wherein L_A is the length of the amplicon A; and wherein L_L is the length of the longest amplicon, and wherein the amplicons are distinct.

10. The method of claim 9 wherein the primers are present in the following molar ratios: exon 2 (89.4): exon 3 (26.9): exon 4 (450): exon 5 (245.8): exon 6 (138.3): exon 7 (101.8): exon 8 (193.0): exon 9 (70.8): exon 10 (146.5): exon 11 (177.3).

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priming DNA synthesis on a genomic p53 template in a vessel with ten sets of

primers which amplify exons 2-11 of p53, wherein the primers are shown in SEQ ID NOS: 1-20, wherein the primers are present in the vessel at the following molar ratios: exon 2 (89.4), exon 3 (26.9), exon 4 (450), exon 5 (245.8), exon 6 (138.3), exon 7 (101.8), exon 8 (193.0), exon 9 (70.8), exon 10 (146.5), exon 11 (177.3).

13. (Amended) The kit of claim 12 wherein the molar ratio of the concentrations of the primers is described by:

$$C_A = C_L (L_A \div L_L)^2$$

wherein C_A is the concentration of primers for an amplicon A; wherein C_L is the concentration of primer for the longest amplicon; wherein L_A is the length of the amplicon A; and wherein L_L is the length of the longest amplicon.

15. (Amended) A [mixture] composition of primers for performing multiplex polymerase chain reaction of at least two amplicons, wherein the primers [are present in the] consist of a mixture at a predetermined molar ratio to each other, wherein the molar ratio of the concentrations of the primers is described by:

$$C_A = C_L (L_A \div L_L)^2$$

wherein C_A is the concentration of primers for an amplicon A; wherein C_L is the concentration of primer for the longest amplicon; wherein L_A is the length of the amplicon A; and wherein L_L is the length of the longest amplicon, wherein the amplicons are distinct.